

SCIENTIFIC CORRESPONDENCE

Elevated cortisol levels and increased rates of diabetes and mood symptoms in Soviet Union-born Jewish immigrants to Germany

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SIR—Environmental and emotional stressors are associated with persistent activation of the endogenous glucocorticoid system. Chronic hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis is a contributing factor both to metabolic diseases, including diabetes mellitus, and to psychiatric disorders, such as depression and anxiety.^{1–3} Surveys of phenomenology, comorbidity, family history, genetic traits, and pharmacologic treatment responses of mood disorders and the metabolic syndrome suggest that both types of condition may overlap and share striking similarities.^{4–6} Little is known about the causal relationships and the initial sequence of events triggering and sustaining these complex and inter-related processes. In order to assess the contributions of environmental and lifestyle changes to these two outcomes, we studied a defined ethnic population following immigration with marked changes in social environment. It is reasonable to assume that increased mobility and immigration leading to profound alterations in culture and social structures result in drastic alterations in lifestyle and consequent exposure to long-lasting stress.

Immigration into Western societies accelerates the development of the metabolic syndrome in certain ethnic groups. For example, Indian migrants living in the USA or UK have higher prevalence rates of diabetes, coronary heart disease (CHD) and dyslipidemia compared to native populations.^{7–9} This process has been particularly alarming with an accelerated or premature CHD in relatively young individuals. The cause of these clinical observations has been attributed to the obvious changes in lifestyle and diet as well as the distinct genetic background of the diverse populations. Although this hypothesis appears reasonable, it may be too simplistic to fully explain this phenomenon.

Recent evidence suggests that increased serum cortisol concentrations may contribute to ethnic differences in the prevalence of the metabolic syndrome, particularly among the obese.¹⁰ We therefore analyzed the occurrence of the metabolic syndrome, the cortisol response to awakening, and mood

symptoms in two distinct populations of immigrants from the former Soviet Union to Germany. We studied 598 Russian-speaking Jewish immigrants (JI, contingent refugees) and 86 Russian-speaking immigrants with German family background (RG), who were compared to 2428 native German (NG) citizens with respect to the prevalence of diabetes, the major constituent of the metabolic syndrome (Figure 1a). Only immigrants who came to Germany during the last 6 years were included in the study.

In order to analyze the stress response, free cortisol levels after awakening, which are a reliable biological marker for the assessment of adrenocortical activity, were assessed using salivary samples. Results were expressed as area under the curve (AUC).^{11,12} Compliance was assured with the SmartCap system (MEMS V, Medical event monitoring system), as described previously (Figure 1b).¹³ All subjects were studied in the same outpatient community care practice by the same physician. Medical data and psychosocial assessments were performed in the appropriate native language. Patients were scored for depression and anxiety on the General Health Questionnaire (Figure 1c).¹⁴

We found that in comparison to NG subjects or RG, the population of JI had the highest rates of all three assessed parameters (diabetes mellitus 10.4%; salivary cortisol awakening response 31.4 ± 3.3 nmol/l/h; anxiety and depression scores 10.54 ± 0.45 and 7.34 ± 0.64). In contrast, the prevalence rates of diabetes (6.8 vs 5.8%) and salivary cortisol awakening response (23.3 ± 1.9 vs 21.6 ± 1.4 nmol/l/h) did not differ between the groups of NG subjects and RG (Figure 1a and b). The anxiety/depression scores of RG (8.77 ± 0.63 and 4.65 ± 0.86) was in between the scores of NG (5.96 ± 0.64 and 1.83 ± 0.74) and that of JI (10.54 ± 0.45 and 7.34 ± 0.64) (Figure 1c). These data suggest that migration *per se* is associated with increased psychological burden manifesting as mood and anxiety symptoms.

The fact that only the JI have an increased prevalence of diabetes and increased concentration of salivary cortisol may be attributed to some specific circumstances. For example, while the majority of RG come from the rural areas of the former Soviet Union, Russian-speaking JI used to predominantly live in urban communities, thereby being exposed to different lifestyles and diets. The significantly increased levels of cortisol in JI living in Germany may also reflect prior personal or familial exposure to a specific emotional stressor, namely the Holocaust, inflicted by Germany's former Nazi government. This particular constellation of stress may also culminate in metabolic complications as reflected in an increased prevalence rate of diabetes in this population.

In conclusion, these data suggest that immigrant populations should be carefully screened in order

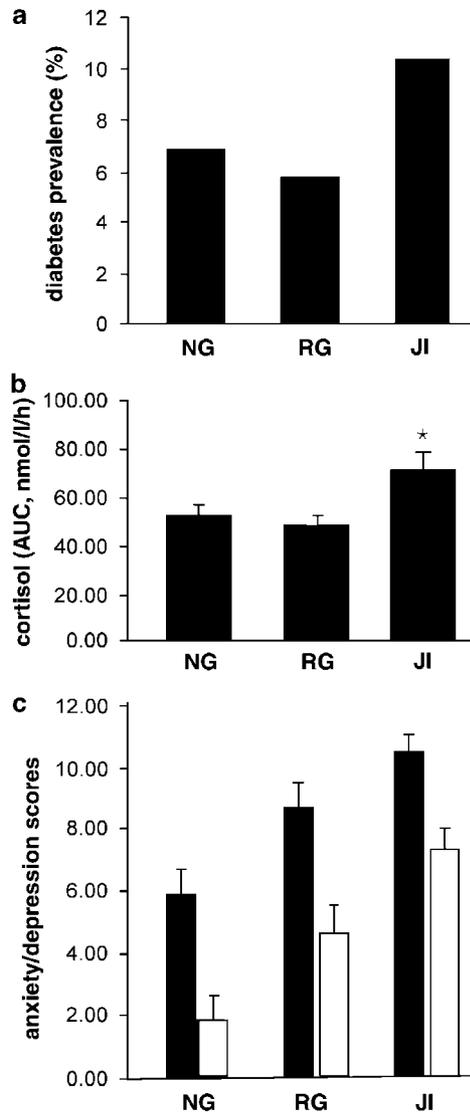


Figure 1 (a) Prevalence (%) of diabetes in native German subjects (NG, $n=2428$) as compared to post-Soviet immigrants with Jewish (JI, $n=598$) and Russian-German (RG, $n=86$) family background. (b) Morning saliva free cortisol levels in NG subjects ($n=20$), immigrants with Jewish ($n=19$) and RG ($n=14$) family background. The three groups were matched for age and gender distribution. Saliva samples were collected immediately after waking up, 30 and 45 min later (Salivetten; Sarstedt, Germany) and free cortisol levels were measured using a commercially available immunoassay (IBL, Hamburg, Germany). Electronic monitor caps provided an objective date and time stamp of each sample thereby verifying compliance of the participants. Values are expressed as mean area under the curve (AUC). (c) Anxiety score (black bars) and depression score (white bars) in all three populations studied (NG, $n=24$; RG, $n=26$; JI, $n=56$). Data are expressed as means \pm SE; * $P<0.05$ vs NG. Differences between mean values were tested for statistical significance by analysis of variance (ANOVA).

to facilitate early diagnosis and prevention of stress-related psychiatric and metabolic disorders. Future studies should examine the roles of specific gene–environment interactions in the pathogenesis of the metabolic syndrome among immigrant populations.

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Depression and anxiety symptoms in diabetic patients on continuous subcutaneous insulin infusion (CSII)

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SIR—Diabetes mellitus is associated with depression, anxiety, tension, and current perceived stress.^{1,2} In diabetics, symptoms of depression have been associated with increased complications. Reducing the